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THE TREATMENT OF LEPROSY.

WITH ESPECIAL REFERENCE TO SOME NEW CHAULMOOGRA OIL DERIVATIVES.

By J. T. McDONALD, A. M., M. D., Director, Leprosy Investigation Station, United States Public Health Service, and Superintending Physician to Kalihi Hospital, Hawaii; and A. L. DEAN, A. B., Ph. D., President and Professor of Chemistry, University of Hawaii, Honolulu.

Leprosy not an incurable disease.

From a careful review of the medical literature upon the subject for the past decade or two, one can not avoid the conviction that there has arisen a new confidence in the curability of leprosy. Unna delivered an address upon "La Pathologie et la Thérapeutique de la Lèpre," in which he declares that the time has happily gone by when, according to common opinion, leprosy was considered incurable, and when every physician who would not permit himself to be tyrannized by that disheartening dogma was met only by a charitable smile. He declared that leprosy was making its way on the same ground as tuberculosis and that it was only the persistent, faithful work of a few physicians who were not satisfied with that easy-going doctrine that had brought about the hopeful change.[1]

Unna's dicta and opinions have been respected and frequently quoted by writers upon the subject the world over. It is a significant fact that at the Second International Conference on Leprosy, held in Bergen, Norway, in 1909, at which this Station was represented by its Director, the late lamented Surg. Donald H. Currie, United States Public Health Service, that body declared by formal resolution that "The clinical study of leprosy induces the belief that it is not incurable."[2] So many successful results are to-day being obtained in the treatment of the disease in various parts of the world, that the statement still occasionally seen that leprosy is incurable is, to say the least, an anachronism.

This paper will recite briefly the methods of treatment we have found useful.

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[1] Les temps sont heureusement passés, où, d'après l'opinion universelle, la lèpre était incurable, où chaque médecin qui ne se laissait pas tyranniser par ce dogme désolant ne recueillait qu'un sourire charitable. La lèpre a fait, en cela, le même chemin que la tuberculose. Ce n'ont été que les bons succès de quelques médecins, qui ne se contentaient pas de ce "dogme de commodité," qui y ont produit un changement.—XV Congrès International de Médecine: Lisbonne, 1906, Section VIII, Dermatologie et Syphiligraphie, 2 me fascicule, p. 310.

[2] Public Health Reports, Vol. XXIV, No. 38, p. 1357.

General Measures in Treatment of Leprosy.

As a prerequisite to, and combined with, specific medication, especial importance is placed upon the general welfare of the patients. The food is of good quality, ample, well-cooked, and well-served in cheery dining rooms. In the dormitories, the patients care for their own rooms and are held to account for neatness and cleanliness both in person and in surroundings. Idleness is discouraged and meditative moping is not permitted. The adult males find occupation and diversion in vegetable and flower gardening, care of the live stock, repairs and painting, upkeep of lawns, etc., and the women busy themselves with the usual activities of home life, except the cooking and serving of meals. The younger boys and girls attend school a few hours daily under a teacher patient, and behave during the rest of the time precisely as do children everywhere. The entire community plays tennis, baseball, volley ball, basket ball, croquet, billiards, etc., and in the evenings, dances and movies in the Assembly Hall are of frequent occurrence. The patients have their own stringed orchestra and singing club and every few weeks stage a play or a concert with costumes of their own design and making. There is a spirit of good cheer and hopefulness, each one determined to achieve a cure. Cases which improve to the point where the clinical signs have disappeared and the bacillus can no longer be demonstrated are recommended for parole by the physician in charge. A board of three physicians is appointed by the board of health and this board passes on the advisability of allowing the patient to go out, as no longer a menace to the public health. Paroled patients are required to report at stated intervals. The care received, the spectacle of fellow patients being paroled, and the general atmosphere of the hospital lead to a high state of morale; such effects on physiological tone as may be due to mental condition are highly favorable.

On the arrival of new patients at the hospital, after their official examination and formal admission, our first care is to give them a thorough examination to learn what they need to improve their general condition. For instance, those who seem to be badly nourished and anemic are immediately put upon some standard tonic, such as a tablet of iron, arsenious acid, and strychnine. We find that they quickly respond to the improved surroundings, good care, and treatment, by improved appetite, gain in weight, etc. We believe this puts them in a better state to receive and assimilate the remedies directed specifically to the cure of the disease. Others, again, enter with scabies, which is promptly relieved by sulphur ointment applied in the usual way. Ulcers respond kindly to appropriate treatment and heal in a few weeks. Briefly, our object is to put and maintain every patient in as good general health as possible.

Of the long list of drugs and remedies used especially against leprosy by various authorities we have nothing derogatory to state. The writers have great faith in strychnine, recommended by Dyer and Hopkins of New Orleans, as we certainly have had good results from its constant use, especially in nerve cases. Arsenious acid, gurjun oil, and several others of the old-time remedies, so far as tried, have maintained their good reputation in our hands, and we believe have done good.

The Use of Chaulmoogra Oil.

The remedy to which we pin our faith as superior to all others is chaulmoogra oil. For many years it was used in Hawaii in its crude state, with results very similar to those obtained elsewhere. To the majority of patients it is nauseating and offensive to the stomach even when taken in slowly increasing doses by capsules, and its use has to be discontinued for a time, to be begun later at a diminished dose. Given intramuscularly it is painful and slow of absorption.

Many attempts at its modification have met with more or less success according to reports from various sources, and one report which has attracted especial attention is that of Dr. Victor G. Heiser, surgeon, United States Public Health Service, director of health for the Philippine Islands, published in 1914.[3] Although the report covers but 12 cases, it is mentioned in this connection because it seems to have been the starting point of an awakened interest and especial effort in the Orient, where the treatment was tried with favorable results in various missionary hospitals in India and China. The Heiser formula is as follows:

Chaulmoogra oil	cc.	60
Camphorated oil	cc.	60
Resorcin	grams.	4

Mix and dissolve with the aid of heat on a water bath and then filter.

It is used intramuscularly and "the injections are usually made at weekly intervals in ascending doses. The initial dose is 1 cc., and this is increased to the point of tolerance."

A review of the earlier literature covering the use of chaulmoogra oil may be found in United States Public Health Service Bulletin No. 75, January, 1916, by Surg. G. W. McCoy and Acting Asst. Surg. Harry T. Hollmann. Their summary of this review is as follows:

"Our personal experience leads us to the conclusion that most writers have reached—that the oil is helpful to many cases of leprosy, perhaps the majority.

"The hypodermic method of administration, while not free from disagreeable complications, seems to have given good results, and, in view of the nature of the disease, ought to be given a further trial.

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[3] Public Health Reports, vol. 29, No. 42, p. 2733.

"We are sure that the use of chaulmoogra oil as at present practiced is not the solution of the problem of the therapeutics of leprosy."

The use of injections of mixtures containing crude chaulmoogra oil along the lines reported by Heiser had given sufficiently encouraging results to stimulate further investigation, and was continued at the Kalihi Hospital in the period following the work reported in Bulletin 75.

A mixture of the following composition was employed:

Formula No. 1.

Chaulmoogra oil	cc..	500
Olive oil	cc..	500
Camphor	grams..	5
Guaiacol	do....	10

This method of treatment was employed on many patients with generally favorable results. In most cases the oil was given by mouth as well as by the intramuscular route. The amount of oil which could be tolerated in this way varied considerably with individuals. The practice was to increase the dosage until the limit of tolerance was approximately reached. Lugol's solution, which was frequently administered, was likewise varied in doses, beginning with small amounts and gradually working the dosage up until the patient was receiving substantial quantities of iodine in this form.

This combination of intramuscular and oral administration was beneficial in the majority of cases, and in a number of them resulted in the patient's becoming apparently bacteriologically negative and being paroled from the hospital. A report covering 12 of these paroled cases is given by Hollmann.[4] In the great majority of cases which became bacteriologically negative, there has been no reappearance of the disease.

The results obtained by Heiser, and by the various members of the staff of the Leprosy Investigation Station here in Honolulu, gave one of us (A. L. D.) good reason to believe that in chaulmoogra oil there were one or more active principles which had a specific action in leprosy. It seemed clear that this active agent is much more effective when introduced into the body hypodermically or intramuscularly than when taken by mouth. Nevertheless the action of the injected mixtures of the crude oil is slow, the injections are painful, and the material is usually slowly absorbed. Further progress in the development of the treatment of leprosy by use of chaulmoogra oil appeared to depend upon chemical and clinical investigations directed to the isolation of the active principle and its more efficient application. There were, therefore, problems, both chemical and physiological, requiring the application of experimental methods. There was, however, the broader problem of the development of the best system of medical treatment for leprosy, which involves not only these scientific aspects of the problem, but also the most advantageous application of any other agencies likely to lead to a more rapid and complete mastery of the disease.

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[4] Journal of Cutaneous Diseases, vol. 37, pp. 367-373.

CHAULMOOGRA OIL DERIVATIVES.

Chaulmoogra oil is one of the few members of the group of fatty oils which are believed to have distinct physiological effects outside of their nutritive value. The fatty oils are of great physiological importance, but, heretofore, chiefly in relation to nutrition and the general metabolism of the body. In a series of papers from the Wellcome Research Laboratory, by Power and his collaborators,[5] the constitution of chaulmoogra oil and some of the closely related oils was elucidated. They discovered a new series of fatty acids represented by two members—chaulmoogric acid, $C_{18}H_{32}0_2$, and hydnocarpic acid, $C_{16}H_{28}0_2$. These acids differ from any other known fatty acids in that they rotate the plane of polarized light to a notable degree—chaulmoogric acid $[a]_D = +62.1^\circ$ and hydnocarpic acid $[a]_D = +68^\circ$. The studies on their constitution indicated that each of these acids contains a five-carbon-ring nucleus. Both of these acids were isolated from chaulmoogra oil derived from the seeds of *Taraktogenos kurzii*, and also from the oil of closely related species belonging to the genus Hydnocarpus. Power and his coworkers did not concern themselves with the therapeutic use of chaulmoogra oil.

It would appear possible that the distinctive action of chaulmoogra oil, as heretofore reported, may be due either to the glycerides of the unique fatty acids of chaulmoogra oil or to the presence of some other oil-soluble constituent not a glyceride. The first step in the attempt to identify the active agents would be the separating of chaulmoogra oil into fractions and the use of these fractions on groups of lepers. The separating of the glyceride mixtures which make up the various vegetable fatty oils is very difficult; the fatty acids obtained by the decomposition of the glycerides are somewhat more readily separated.

Sir Leonard Rogers, in his experiments using the intravenous injections of the sodium salts of the acids derived from chaulmoogra oil, made use of fractions, separated by Ghosh.[6] The data presented by Ghosh showed clearly that he was dealing with mixtures of fatty acids, and probably very complicated mixtures. The separation of the constituent fatty acids from the mixed product derived from the saponification of chaulmoogra oil by means of fractional crystallization is a tedious and complicated task, and Ghosh did not meet with much success.

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[5] Power and Gornall, The Constituents of Chaulmoogra Seeds: Jour. Chem. Soc. LXXXV, p. 838 (1904); Power and Gornall, The Constitution of Chaulmoogric Acid: Jour. Chem. Soc. LXXXV, p. 851 (1904); Power and Barrowcliff, The Constituents of the Seeds of Hydnocarpus Wightiana and of Hydnocarpus Anthelmintica—Isolation of a Homologue of Chaulmoogric Acid: Jour. Chem. Soc. LXXXVII, p. 884 (1905); Barrowcliff and Power, The Constitution of Chaulmoogric and Hydnocarpic Acids: Jour. Chem. Soc. XCI, p. 557 (1907).

[6] Sudhamoy Ghosh, M. SC. (Cal.), D. SC. (Edin.), F. C. S. (London), Report of a Chemical Investigation of Chaulmoogra Oil in Connection with Leprosy Treatment: Indian Jour. Med. Research, IV, p. 691 (1916).

It is quite clear from the results heretofore published that although there is a therapeutic agent (or agents) in chaulmoogra oil of marked value in leprosy, none of the attempts to isolate or identify this agent has led to conclusive results.

A recent publication of Sir Leonard Rogers[7] describes the use of "gynocardate of soda" and "morrhuate of soda." His term "morrhuate of soda" refers to the sodium soaps of the fatty acids of cod-liver oil, and he reports excellent results from the intravenous and hypodermic injections of this material. The fatty acids of cod-liver oil are of a peculiar and unusual type, although not of the chaulmoogric series. If the results of Rogers are confirmed, it will appear that the fatty acids of cod-liver oil are also useful in leprosy. Although it may be, as suggested by Rogers, that "other unsaturated fatty acids may also be expected to yield effective preparations against the acid-fast bacilli of both leprosy and tuberculosis," it seems to us unlikely that this is a property common to all unsaturated fatty acids. For example, oleic acid, which is unsaturated to the same extent as chaulmoogric acid, is a common body constituent, and it would therefore be rather improbable that weekly injections of, say, 5 cc. of a 3 per cent solution of sodium oleate, amounting to 0.15 gram dry material, would have any such effect in leprosy as has been reported following the use of even smaller quantities of the sodium soaps of the fatty acids of chaulmoogra oil. Obviously a wide and important field for chemical and physiological investigation has been opened by this work of Sir Leonard Rogers and our own work here.

As an initial step, the fatty acids of chaulmoogra oil were separated into four fractions in the chemical laboratory of the College of Hawaii. One of these fractions was chaulmoogric acid, and the other three were mixtures of acids having somewhat different properties. These fatty acid fractions are solids, and therefore unavailable directly for hypodermic or intramuscular injections. One of the first problems was to find a suitable form of material for injection which would allow rapid absorption into the circulation. It was found that the ethyl esters of the fatty acids were thin-fluid oils lending themselves readily to intramuscular injections and were readily absorbed.

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[7] Paper read before the Medical Section of The Asiatic Society of Bengal, Mar. 12, 1919, by Sir Leonard Rogers, M. D., F. R. C. P., F. R. C. S., Lieutenant Colonel, I. M. S.

The four fractions originally tried out, and designated, respectively, "A," "B," "C," and "D," were of the following character:

Fraction "A": The ethyl ester of chaulmoogric acid.

Fraction "B": The ethyl esters of the other fatty acids readily separating on cooling the alcoholic solution of the mixed fatty acids of chaulmoogra oil, doubtless containing considerable of "A".

Fraction "C": The ethyl esters of the fatty acids remaining in the mother liquor from the separation of the acids in "A" and "B" and yielding lead salts readily soluble in ether.

Fraction "D": Ethyl esters of the fatty acids accompanying "C" in the alcoholic separation, but yielding lead salts not readily soluble in ether.

The early results of the use of these fractions "A," "B," "C," and "D," together with some details of the methods of their preparation, are given by Hollmann and Dean.[8]

The results published and a continuation of the same lines of work lead to the general conclusion that the therapeutic agent in chaulmoogra oil is able to survive the chemical treatments involved in the making of these preparations and is itself distributed through all four of the fractions. The differences in results, using the different fractions, are not sufficient to warrant any final conclusions regarding their relative efficiency; patients receiving each of the fractions have shown marked improvement, have become bacterially negative, and have been paroled. It is impossible, however, to draw definite conclusions from this work because of the fact that all patients who received the injections also regularly received chaulmoogra oil by mouth in substantial quantities. We can not say, therefore, whether the beneficial action in any particular case is due to the material injected or to the combined action of the material injected and that taken by mouth. The general observation that chaulmoogra oil taken by mouth has a beneficial but not decisive action lends color to the belief that the most important factor in the improvement of the various cases is the injected material. As a series of experiments intended to develop the best method for leprosy treatment the plan followed was satisfactory, but it is not satisfactory as a method of demonstrating the relative efficiency of different fractions of the oil.

DISTILLED ESTERS.

As already indicated, the processes which resulted in the fractions "A," "B," "C," and "D" are of such a character as to make it improbable that any other material except fatty acids would survive them and be distributed in all four of these fractions. Still further evidence on this point was gained by a different system of fractionation. In this case the mixed fatty acids derived from the saponification of chaulmoogra oil were converted into ethyl esters by heating with absolute alcohol in the presence of dry hydrochloric acid gas, giving a mixture of the ethyl esters of all the acids present in the crude oil. This acid mixture was distilled *in vacuo* at a pressure of 30 to 34 mm. The distillate was cut into three fractions of different boiling ranges, designated "E," "F," and "G." These distilled esters are colorless liquids. At the time the first work of this character was done no apparatus was available to provide higher vacua and allow satisfactory distillations. The fractions "E," "F," and "G" were used for intramuscular injections in a number of patients, beginning in January, 1919, and in some cases extending until about the 1st of July of that year. It was found that all the cases receiving each one of the fractions "E," "F," and "G" showed improvement—some of them quite rapid—indicating that the methods employed in their production had not resulted in the destruction of the therapeutic agent or agents.

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[8] Journal of Cutaneous Diseases, vol. 37, pp. 367-373.

The same uncertainty surrounds the interpretation of these results as exists in the cases receiving fractions "A," "B," "C," and "D," since all were getting chaulmoogra oil in capsules three times daily in addition to the weekly injections. We can say, however, that whatever virtue resides in the use of chaulmoogra oil derivatives injected intramuscularly in combination with the oral administration, that virtue is probably not lost or segregated to an appreciable extent by any of the chemical or physical conditions to which these various preparations have been exposed.

The use of vacuum distillations as a means of separating the esters of the fatty acids and the fatty acids themselves is receiving extensive application in the chemical investigations now in progress.

THE ADMINISTRATION OF THE ETHYL ESTERS.

The intramuscular injections are given once a week, Wednesday being known as "Injection Day." An adequate supply of injection material, together with syringes, needles, etc., is previously subjected to about 15 pounds of steam pressure for from a half to one hour in the autoclave. Other methods of sterilization would doubtless answer equally as well; for instance, an ordinary kitchen double boiler ought to serve every purpose, especially when only a few patients are to be treated. The patients, instead of dreading what must be a rather painful performance, make a gala day event of it and fill the hour with laughter, noise, and chatter on the lawn outside while awaiting their turns.

The site chosen by us for the injection is the upper and outer quadrant of the gluteal region, alternating sides weekly. One of the patients, who is called the "painter," applies tincture of iodine to a spot the size of a silver dollar. The syringe used is an ordinary 20-cc. all-glass model, and the needle selected is a No. 20, although with the thin and limpid ethyl esters a smaller size would undoubtedly serve. Sterile needles, one for each patient, are in readiness; the material is poured from the flask into a sterile beaker, a patient assistant stands on one side with a previously prepared basin of cotton pledgets, and on the other side is the clerk, usually the laboratory assistant, record book in hand, to enter opposite the name in a properly ruled, dated column the number of cubic centimeters given each patient on that day. A syringe full of the material is drawn up from the beaker, then, with a small spring forceps, a needle is picked up from the large Petri dish containing them and placed on the stem of the syringe. The patients are taught to step lively, and one by one they quickly enter from the preparation room, the needle is passed its whole length to reach the musculature, and the proposed dose is gently administered. The instant the needle is withdrawn the assistant claps a pledget of cotton over the puncture, and the patient's own hand is applied to retain it with a gentle pressure for a few minutes in the preparation room. By the time the operator has removed and discarded the used needle and replaced it by a clean one the next patient is in position. We can thus easily administer from 75 to 100 injections in an hour or two and do it well. Employing 1 cc. as the initial dose, it is our custom at every second or third injection to increase the dose by 1 cc. until we reach a maximum of from 3 to 5 cc., according to the age or weight of the patient.

A phenomenon noted by many other observers in using chaulmoogra oil injections occurs with us also; in a few instances, immediately following the injection, the patient is seized with a violent fit of coughing. It quickly begins to subside, however, and in less than five minutes has entirely disappeared, leaving no serious results.

As to effects, or so-called "reactions" following our injections, there is a considerable diversity of reports. Some claim that during the following 24 hours they experience creeping sensations of chilliness at times, that they are rather out of sorts and feverish, with an indifferent appetite, etc.; others say they do not notice any such symptoms; while all admit a soreness for a day or two, deep under the point of injection. In a few instances we have taken the morning and evening temperature of all the patients on injection day and the day following, with the result that not 3 per cent of the number showed any rise whatever, either on the evening of injection day or morning or evening of the day following. The rise of temperature in those who did show any appreciable rise did not exceed one degree; from which it may be inferred that the constitutional symptoms following our injections are practically nil.

While some have reported from other sources rather frequent abscess formation as derogatory to intramuscular injection of chaulmoogra oil, we are happy to report more favorable results, as in 4,892 deep injections administered from October 1, 1918, to the present writing (January, 1920), we have had but one case of resulting abscess.

COMBINED IODINE IN TREATMENT.

For a number of years iodine has been employed in the treatments, chiefly in the form of Lugol's solution. Since the fatty acids of chaulmoogra oil are for the most part unsaturated acids and therefore capable of adding iodine to form iodine compounds, it seemed possible to utilize this property to introduce iodine into the body either through the skin, by injection, or by way of the mouth. Iodine combined in this way has none of the irritating action of free iodine. We have been employing treatments since February, 1919, in which combined iodine has been used.

In the period between February 5 and March 12, 1919, nine newly received patients were placed in a group to receive injections of a preparation consisting of the mixed ethyl esters of chaulmoogra oil carrying 4 per cent of combined iodine. Subsequently, the percentage of iodine has been varied between 2 and 8 per cent.

In addition to the weekly injections, these patients received capsules three times per day, containing the mixed fatty acids of chaulmoogra oil carrying 5 per cent of combined iodine. The fatty acids were used instead of the oil itself because hydrolysis of the glycerides to fatty acids is the normal digestive process which precedes fat absorption. We were therefore using a predigested oil. We can see no advantage in the use of the sodium salts, as practiced by Rogers, since these soaps would be reconverted into the fatty acids by the hydrochloric acid of the stomach. Between May 14 and June 4, 1919, two additional patients were placed on this treatment. About the last of June it became necessary to ship a considerable number of patients to Molokai on account of the crowded condition at Kalihi. This unfortunately caused the loss of 4 of our 11 patients in this experiment. The remaining 7 have all been paroled. Since the cases sent to Molokai were the less promising ones, they would not have been fit for parole in November, and might, perhaps, never have become bacteriologically negative.

"STANDARD TREATMENT."

Because of the excellent progress which patients were making on the treatment just described it was decided to adopt this as the standard routine practice, placing on this treatment all patients who were received, unless they were to be in some group for special investigation. As already indicated, we have done some shifting about with the proportions of iodine employed, and the standard treatment now consists in weekly injections of a preparation which consists of the mixed ethyl esters of the acids of chaulmoogra oil with 2 per cent of iodine in chemical combination. The amount used starts at 1 cc. and is gradually increased to a maximum of 4 or 5 cc. for adults.

Three times each day, an hour and a half after meals, the patient receives capsules containing the fatty acids of chaulmoogra oil with 2½ per cent of iodine chemically combined. The dosage for the first 15 days is ⅙ gram per 100 pounds of body weight three times daily; for the second half of the first month, ⅓ gram per 100 pounds; for the first half of the second month, ⅔ gram per 100 pounds; and after that, 1 gram per 100 pounds of body weight. This means, for example, that a 150-pound man would get 1½ grams per dose or 4½ grams per day.

In addition to this treatment, the patients also receive such other medical care as may be indicated in each case.

TREATMENT BY INJECTIONS ONLY.

It has already been pointed out that the injection of various preparations has been accompanied by the oral administration of crude chaulmoogra oil or its derivatives. The experiences of others, as set forth in the literature of leprosy, as well as our own observations, point to the conclusion that the oil which passes through the digestive tract plays a minor part in the improvement noted. Much larger quantities are taken by the mouth than by injection; yet, when the injections are not employed, the recovery is slow, uncertain, and incomplete.

In administering treatment on a large scale, great economy of material would be effected by using injections only, and the whole treatment simplified. In order to test the efficacy of the injection feature of our standard treatment without the feature of oral administration of the iodized fatty acids, a group of 10 patients who had recently been admitted to the hospital, and had never received more than very small amounts of chaulmoogra oil, were placed on treatment by injection only. A small dosage of strychnine was given, partly for its tonic effect and partly for the psychological value of having "something to take," like the others. It is too soon to draw final conclusions, but the results to date are very encouraging. Perhaps these patients are not improving quite as rapidly as those on the regular treatment, but they are certainly improving.

ACCESSORY TREATMENTS.

Although experience indicates that the chief factor in the good results we have attained is the intramuscular use of chaulmoogra derivatives, aided by those taken orally, it is nevertheless advantageous to make use of any adjuvant measures which have proved of value. It has been shown that aqueous solutions do not penetrate the sound skin, whereas oily ones enter to greater or less depths.

Iodine liniment.—We have tried the superficial application of a "green oil" consisting of the ethyl esters of chaulmoogra oil, carrying combined iodine amounting to from 10 to 25 per cent by weight. This oil penetrates well, especially when aided by brisk massage. Definite and convincing data covering its value are not available, but it is in considerable demand by the patients, who are given 50 cc. vials and allowed to apply the oil three times daily.

Ointments.—For old and sluggish ulcers as well as for chronic eczematous looking spots and areas which need stimulating, we employ the ointment of ammoniated mercury of the United States Pharmacopœia, which we modify by mixing it with ointment of zinc oxide in equal parts when we desire to render it milder, or, on the other hand, if we have a lesion which requires something stronger, we rub into our ointment of ammoniated mercury a dash of finely powdered salicylic acid, much or little, as the appearance of the lesion seems to indicate. Patients coming in with open sores or ulcers are expected to have them all healed in a few weeks' time, and they seldom disappoint us.

Trichloracetic acid.—While we never use the actual cautery as employed by Unna, we have had excellent results from painting nodules with pure trichloracetic acid, which immediately produces a considerable escharotic action; the skin turns white and there is more or less smarting and burning for a few moments. By the time the effects of the acid treatment have passed off, usually one or two weeks, the nodule is a little softer and a little smaller and the patient is anxious for another application. There is one serious drawback to the use of the acid, noticed also in the case of carbon dioxide snow used here some years ago, and that is its interference with the pigmentation of the part to which it is applied. In some cases the skin is hyperpigmented and in others, hypopigmented. The former is illustrated in the case of a young woman still with us who over a year ago had decided thickenings over each malar region. Several applications entirely cleared up the infiltrations on the cheeks, but, unfortunately, left two unsightly areas, each the size of a silver dollar, almost entirely black. After several weeks, however, they began to fade and now, after many months, they are barely visible. On the other hand, a young man, paroled over a year ago, the lobes of whose ears were similarly treated, has a distinct loss of pigment and it shows no sign of returning.

Nodular injections.—We have been cautiously trying the injection of material which we have employed intramuscularly directly into the leprous nodules. Of course, it is understood that this and the preceding methods are applicable only when the nodules are few; for instance, we have a few patients whose stay with us has been prolonged by the lingering nodular enlargement of the lobe of one or both ears, their other lesions having disappeared. With aseptic precaution, we slowly instil a very few drops in various parts of the nodule, employing for the purpose an ordinary all-glass hypodermic syringe with the same technique as in our intramuscular injections; that is, slipping on a clean sterile needle for each injection. It is evidently rather painful and is followed usually by a considerable swelling which soon subsides, however, leaving the nodule appreciably softer and smaller. We think better progress is being made by the injections than by the external application of the trichloracetic acid. Both are good and each has its use. For a very superficial, hard, nodular area the acid is preferable.

Heliotherapy.—Another accessory treatment used, rather crudely, however, at this hospital, is heliotherapy, or the employment of sun baths. We have had some remarkable cures of ulcerations, including the plantar pedis variety, in presenting them to the direct rays of the sun, but whether it is a case of *post hoc* or *propter hoc*, it is not easy to say. A patient enters the hospital and is found to have an ulcer as large as a silver dollar on the sole of one foot, extending nearly or quite to the bones. He has been a laboring man, on his feet nearly the whole of every day. We discover it only by inspection, for he does not betray its presence by the slightest limp in his walk, for the foot is absolutely anesthetic. He is slightly anemic and is put upon our ferruginous tonic; he is put upon our standard treatment of injections and capsules; he is handed a pair of crutches and absolutely forbidden to put a pound of weight on the foot affected or touch it to the ground in moving about. He gets his ulcer washed out every day with a permanganate solution. He gets three good meals a day, a good clean bed to sleep in by night, and all the rest and relaxation he desires by day. That ulcer begins at once to heal, sun bath or no sun bath. The sun-bath measure, however, is very popular with our patients. They have more faith in it, perhaps, than has their medical attendant; but no matter, sunshine is abundant and inexpensive, and as yet untouched by the high cost of living. The one great thing is that the ulcers fill and close. The above is not a fanciful picture, but one of constant occurrence with us; and we are ready to admit that heliotherapy is a therapeutic aid of no inconsiderable value. In cases of rebellious plantar ulcers, however, especially with necrotic tissues, nothing approaches in efficacy the operation of Goodhue of Molokai in thorough ablation of the affected parts and allowing the wound to heal by granulation.

NEURAL LEPROSY.

Cases of leprosy of the nerve type are likely to be ignored at institutions so far as treatment is concerned, and attention is likely to be concentrated on nodular cases.

In view of our success during the past year with several instances of the neural type of leprosy, the conviction has forced itself upon us that it is highly important that all these cases should be brought in and subjected to the regular routine treatment for a course of several months at least, especially in the case of children or even of adults of more recent attack. We believe our remedies arrest the disease and prevent further destruction of hands and fingers, even when, as in long-standing cases, normal function can not be fully restored.

But during the past year we have done better than simply arrest the destructive process; we have had the great satisfaction of seeing marked improvement in a considerable number of these purely neural cases, and apparently a complete recovery in others. One young man who came in with a decidedly ataxic gait, unable to raise his body on his toes and with one hand so weak and deformed that he had been compelled to abandon the use of the typewriter a year before entering, so far improved before his parole that his disability in walking had not only disappeared but he became one of the leading tennis players and one of the swiftest runners in the compound. He has now returned to full and efficient clerical duty in an office. A woman with all fingers absorbed to less than half their original length, after a year's treatment, became able to write, to sew and knit, and to execute many movements and functions of which she had for years been deprived. We have had several cases of young men and boys who, on entering, were absolutely unable to button or unbutton their clothing and were compelled to accept the assistance of their fellow patients, but who, after a few months' treatment, became entirely independent and self-reliant in that respect. We have some young women and girls who entered with little and ring fingers partially crooked, who are now able voluntarily to straighten them after many months of inability to do so.

GENERAL RESULTS.

The number of patients during the period from October 1, 1918, to December 31, 1919, were as follows:

Number of patients, October 1, 1918	52
New patients received	134
Total number of cases	186

Deaths	5
Transferred to Molokai	60
Sent to Orient	1
Paroled	48
Total deaths and departures	114
Number of patients, December 31, 1919	72

It will be noted that a little over 25 per cent of all patients who have been in the hospital in the period under review were paroled as apparently clinically and bacteriologically free from the disease, and of the total departures, 42 per cent were by the parole route. Many of those sent to Molokai were not sent because we regarded them as hopeless cases, but because the hospital was overcrowded.

CONCLUSIONS.

The following conclusions may be drawn from our recent experience in the treatment of leprosy:

1. The intramuscular injection of the ethyl esters of the fatty acids of chaulmoogra oil usually leads to a rapid improvement in the clinical symptoms of leprosy. In many cases the lesions disappear, except for scars and permanent injuries, and the leprosy bacillus can no longer be demonstrated.
2. When combined with iodine, the fatty acids of chaulmoogra oil and their esters give good results; but there is no adequate experimental proof that this addition of iodine causes any increase in the effectiveness of the materials used.
3. All of the available evidence obtained from the use of fractions of the fatty acids of chaulmoogra oil indicates that the therapeutic action is due to one or more of the fatty acids of the oil or to some as yet unidentified substance associated therewith. The various methods of fractionation heretofore employed have failed to demonstrate the active agent.
4. Although conclusive evidence is not at hand, it is probable that the oral administration of chaulmoogra oil derivatives is of minor importance compared with the injections.
5. In treating leprosy, it is important to make use of all auxiliary agencies to build up and maintain bodily vigor.
6. Hypodermic injections of the ethyl esters into leprous nodules are followed by marked swelling with ultimate recession of the lesions. This is a valuable auxiliary treatment for especially resistant lesions.

Summary.

It has been sufficiently established that chaulmoogra oil contains one or more agents which exert a marked therapeutic action in many cases of leprosy. We can not say as yet that the disease is cured, since we have no test adequate to establish such a verdict. Whether or not the apparent cures are real and permanent, it is evident that we have a valuable agent at our disposal in the control of the disease.

ON THE POSSIBILITIES OF USING MOSQUITO TRAPS IN ANTIMALARIA WORK.

By C. W. METZ, Carnegie Institution of Washington, Collaborating Biologist, United States Public Health Service.

It appears to the writer that the eradication or control of malaria in the United States is rapidly becoming, if it has not already become, essentially a rural problem, centering around the relatively isolated farmhouse. Here the operations of draining and oiling that are practicable and efficient in urban districts can not be applied on any adequate scale under present economic conditions. Screening is likewise subject to grave practical disadvantages as a wholesale measure, partly because the effective use of screens would necessitate as a prerequisite the rebuilding of a good proportion of the houses to be protected. On the other hand, if elimination of malaria be attempted through treatment of the human host, equal practical difficulties are encountered. To what, then, can we look for any hopeful line of attack on this problem?

One possibility suggests itself when one considers the fact that the focal point of the danger is the farmhouse itself. It seems safe to say that the malaria plasmodia are transmitted from man to mosquito and from mosquito to man mainly indoors or about the house. This means that, in general, the only dangerous mosquitoes are those in or near dwellings. Consequently, if some method could be devised for eradicating or materially reducing the number of these it ought to prove an effective agent in lessening malaria transmission.

Obviously the simplest manner of doing this would be by means of traps or poison, provided they were effective. In all probability both have been tried many times in the past, for the method is too simple and easy not to have received attention from tormented sufferers or others; but the fact remains that no practical exterminator has resulted. This may be because the habits of Anopheles are not such as to make them sufficiently susceptible to baits or traps, or it may be because the subject has not received adequate consideration. I venture to believe the latter, or at least to believe that the matter merits further attention and study, especially from the viewpoint of the biology of the mosquito.

With these features in mind a few preliminary observations and experiments were undertaken in 1918, but they were discontinued